microfluidic channels are fabricated on the cover slip. The channels are patterned in such a way that when the cover slip is positioned over the microarray substrate, each probe column or row falls into a particular fluidic channel. A seal between the cover slip and the substrate slide can be formed by providing a thin gasket layer between the cover slide and the substrate slide. In this way, sample solutions can be pumped into and guided by the channels to interact with each probe along the channels.

[0198] The fluidic channels can be fabricated in the cover slip, for example, by etching a flat substrate or by a direct molding process. Many different channel designs are possible. **FIGS. 37 and 38** illustrate two specific channel designs. Channels are linked to a reservoir at each end, either directly or through other channels. Each reservoir is exposed to a pressure chamber. By generating a pressure difference between the two pressure chambers, the sample liquid is driven back and forth through the channels, as illustrated in **FIG. 39**. A thorough interaction between the sample and probe can be achieved in an orderly fashion. Pressure can be generated in the pressure chamber by either pumping a gas or immiscible liquid in and out of the chambers. Alternatively a voltage can be applied between the two reservoirs that drives the target molecules back and forth through the microfluidic channels by electrophoresis mechanism.

[0199] As illustrated in **FIG. 40**, the micro-channels may in one embodiment of the invention form periodical spatial patterns across the entire microarray. The pitch of the micro-channel pattern can be equal to or much smaller than the size of a spot on the microarray. Assuming that the diameter of a probe spot on the microarray is D and the pitch of the microarray is P, the pitch of the micro-channels, p, can be P or D; or preferably 0.5D; or preferably, 0.2D; or more preferably 0.1D; or 0.05D; or 0.01D. The depth of the micro-channel, h, can be anything ranging from 10D to 0.0001D. The width of the micro-channel, w, can range from 99% to 1% of the pitch. When the micro-channel pitch is close to D, the width of the channel should take more than 90% of the pitch to ensure that most areas of a spot is covered by a channel. In a particular embodiment, the surfaces in the trenches of the microarray are made highly hydrophilic while the top of the "ridge" surface between two adjacent micro-channels is made hydrophobic **(FIG. 41)**.

[0200] The micro-channels can have different spatial patterns across the surface of the cover slip. **FIG. 42** shows a number of different designs. In **FIG. 42***a*, the micro-channels are connected into a single channel zig-zag across the surface. In **FIG. 42***b*, an array of parallel micro-channels are provided across the surface of the microarray. In **FIG. 42***c*, the micro-channels are cross-connected to form a two-dimensional matrix of micro-channels. **FIG. 42***d* shows another configuration of the two-dimensional cross-connected micro-channels, where the "ridges" are positioned to provide random or semi-random distribution of flow. Ridges in this configuration can be bumps, which can have different three-dimensional shapes, such as columns, diamonds, hemispheres, etc. Ridges in this configuration can be high enough that they are in contact with the microarray surface when the cover slip is placed on the microarray with the ridges facing the microarray surface. Alternatively, ridges can be lower so that they are not in contact with the microarray surface when the cover slip is placed on the microarray with the ridges facing the microarray surface. In this situation, ridges can help create turbulent flow of the liquid, and hybridization sensitivity and efficiency can be improved.

[0201] The cover slip can be made of any suitable material including, for example, glass, silicon, polymer, ceramic and metal. The micro-channels can be made of the same material as the cover slip or they can be made of a different material that is laminated or deposited on the cover slip substrate. The material forming the micro-channel can be hard or relatively soft (for example, polydimethyl siloxane (PDMS)). The micro-channel structure can be fabricated using, for example, one of the following micro-fabrication methods: etching (dry or wet), hot embossing, injection molding, micro-electronic discharge machining (EDM) or soft lithography. For example, the micro-channels can be fabricated in the cover slip by etching a flat substrate using precision etching as is found in semiconductor manufacturing. Alternatively, the micro-channels can be fabricated by pressing a patterned plate on the surface of the cover slip material at a temperature high enough to emboss the pattern of the plate onto the cover slip surface. The micro-channels can also be fabricated by injecting the molten substrate material and cooling the material in the mold.

[0202] In one embodiment of the invention, a clamping force can be exerted to the microarray substrate and the cover slip to ensure that the "ridges" of the micro-channel field are in firm contact with the microarray surface, as illustrated in **FIG. 40**. The sample liquid can be introduced into the channels before or after the placement of cover slip onto the microarray and it is pumped back and forth through the micro-channels during the hybridization.

[0203] To facilitate liquid pumping, reservoirs in fluid communication with the micro-channels can be formed on the cover slip. Liquid flow through the micro-channels can be generated by applying a positive or negative pressure to these reservoirs. There can be, for example, two reservoirs at each end of the cover slip, as shown in FIGS. **42-43**. In other embodiments, more than two reservoirs are possible.

[0204] **FIG. 43** shows one embodiment in which two reservoirs are provided at two ends of the cover slip. Each of these reservoirs includes a through hole connecting the reservoir to the surface of the cover slip opposite the hybridization chamber. On one end, a capillary is inserted into the hole and secured in place. The interior of the capillary therefore becomes part of the reservoir and can receive sample liquid that has passed through the micro-channels. At the opposite end, the other reservoir is coupled with a pressure control source, which provides a positive or negative pressure on that reservoir to cause the sample liquid to flow through the micro-channel. The position of the liquid-air interface in the capillary can be used to measure the volume of liquid that has been pumped through the micro-channels. The measurement can be used to maintain consistency between hybridizations and allow for repeatable hybridization processes.

[0205] In some cases, the area on the probe spot that is under the "ridge" part of the micro-channel may not produce any signal because it does not contact the sample liquid. However, in most microarray applications, the probe molecules are in vast over supply in comparison to sample molecules. Therefore, the portion of the probe spot covered by the "ridge" portion does not have a detrimental effect on